REMARKS

The specification has been amended to delete non-ASCII files from the Computer Program Listing Appendix and to insert sequence ID numbers. Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Please delete the Computer Program Listing Appendix submitted with the original application and enter the enclosed Computer Program Listing Appendix contained on two identical compact discs. A separate transmittal letter for the compact discs is enclosed. No new matter has been added.

Also enclosed are 1) a paper copy of the initial "Sequence Listing"; 2) an computer readable form of the initial "Sequence Listing" on a 3.5" floppy disk; and 3) a statement that the content of the sequence listing information recorded in computer readable form is identical to the written sequence listing and contains no new matter. Please enter the enclosed initial "Sequence Listing" in the application.

Should there be any questions regarding this application, the examiner is invited to contact the undersigned attorney at the number shown below.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Paragraph beginning at page 1, line 10 has been amended as follows:

REFERENCE TO COMPUTER PROGRAM LISTING APPENDIX

A Computer Program Listing Appendix is hereby expressly incorporated by reference. The Computer Program Listing Appendix includes two duplicate compact discs. The files on each compact disc, the date created and the file size in bytes are:

File Name	Date Created	Size (bytes)
[Distribution < DIRECTORY >		
Blank.xls	03/17/2000	34,816
BlankLibrary.xls	07/25/2001	70,144
Getting Started.doc	09/18/2001	41,472
Quick Start.doc	09/14/2001	25,088
SubtractionLibraryUtilityProgramUser'sManual.doc	07/25/2001	190,976
SubtractionLibraryUtility.exe	07/25/2001	360,960
TUTORIAL007.Seq	06/11/2001	604
TUTORIAL008.Seq	06/11/2001	632
TUTORIAL005.Seq	06/11/2001	684
TUTORIAL009.Seq	06/11/2001	647
TUTORIAL006.Seq	06/11/2001	686
TUTORIAL013.Seq	06/11/2001	1,188
TUTORIAL017.Seq	06/11/2001	666
TUTORIAL020.Seq	06/11/2001	611
TUTORIAL010.Seq	06/11/2001	642
TUTORIAL014.Seq	06/11/2001	614
TUTORIAL018.Seq	06/11/2001	617
TUTORIAL011.Seq	06/11/2001	892
TUTORIAL015.Seq	06/11/2001	657
TUTORIAL019.Seq	06/11/2001	665

TUTORIAL012.Seq	06/11/2001	619
TUTORIAL016.Seq	06/11/2001	641
TUTORIAL005r.Seq	06/11/2001	614
TUTORIAL001.Seq	06/11/2001	640
TUTORIAL PRIMERS.VEC	06/08/2001	2,039
TUTORIAL002.Seq	06/11/2001	643
TUTORIAL003.Seq	06/11/2001	627
TUTORIAL004.Seq	06/11/2001	682
Source_code < DIRECTORY >		
SubtractionLibraryUtility < DIRECTORY >]		
MakeHelp.bat	09/27/2000	1,594
newlibrarynamedlg.cpp	10/05/2000	1,926
newlibrarynamedlg.h	09/29/2000	883
resource.h	02/06/2001	8,530
resource.hm	02/06/2001	4,528
startdlg.cpp	10/23/2000	3,742
startdlg.h	10/23/2000	1,093
StdAfx.cpp	10/11/2000	221
StdAfx.h	10/03/2000	602
SubtractionLibraryUtility.cpp	10/11/2000	4,047
SubtractionLibraryUtility.h	02/06/2001	6,385
[SubtractionLibraryUtility.mdp	09/11/2001	42,496]
Subtraction Library Utility.hpj	02/06/2001	2,624
SubtractionLibraryUtility.rc	07/25/2001	28,316
SubtractionLibraryUtilityDlg.cpp	06/21/2001	209,771
SubtractionLibraryUtilityDlg.h	04/16/2001	6,943
Subtraction Library Utility.hm	08/09/2001	663
TimedMessage.cpp	10/27/2000	1,718
TimedMessage.h	0/27/2000	875
trimdialog.cpp	11/06/2000	119,594
trimdialog.h	11/06/2000	4,099

[Hlp <DIRECTORY >		
AfxDlg.doc	10/24/2000	276,992
AfxDlg.rtf	02/07/2001	4,284,257
Copy of SubtractionLibraryUtility.hpj	10/24/2000	2,637
Copy of AfxDlg.rtf	02/07/2001	4,284,257
main.bmp	10/13/2000	709,686
MainScreen.bmp	02/07/2001	718,454
NewLibraryScreen.bmp	10/27/2000	124,374
oldAfxDlg.rtf	02/07/2001	4,284,270
start.bmp	10/16/2000	219,798
SubtractionLibraryUtility.cnt	09/27/2000	157
SUBTRACTIONLIBRARYUTILITY.HLP	08/09/2001	2,115,387
SubtractionLibraryUtility.hm	08/09/2001	663
SubtractionLibraryUtility.hpj	02/06/2001	2,624
SubtractionLibraryUtility.ph	09/27/2000	0
trim.bmp	10/16/2000	1,109,674
TrimScreen.bmp	10/27/2000	1,844,214
word60AfxDlg.doc	10/24/2000	2,171,392
WorkingAfxDlg.rtf	10/30/2000	7,246,340
Res < DIRECTORY >		
SubtractionLibraryUtility.ico	06/11/2001	1,078
SubtractionLibraryUtility.rc2	09/27/2000	417
67 Files Listed: 30,595,230 bytes]		
TUTORIAL PRIMERS.VEC	06/08/2001	2,039
TUTORIAL001.Seq	06/11/2001	640

Paragraph at page 8, line 3, has been amended as follows:

BRIEF DESCRIPTION OF THE DRAWING

Fig. 1 shows a file directory structure for one embodiment of the invention.

Fig. 2 shows a Main User Interface computer display.

Fig. 3 (SEQ ID NOS 7, 9 and 12-16) shows a Trimming Interface computer display.

Table 2. beginning on page 18 has been amended as follows:

Table 2.

```
---------------------------------------------------------------------
Schlager's BLAST UTILITY, RESECO  @1999
Results from file \\r5840\pub\MolTox\blast\TRIMMED\MB2D\M2r02_NV.SEQ
BLAST search done 4/5/2000
---------------------------------------------------------------------------
HTTP/1.0 200 OK MIME-Version: 1.0 Content-type: text/html

    The query sequence for this search has been filtered. Filtering
eliminates low complexity regions that commonly give spuriously high
scores that reflect compositional bias rather than significant position-by-
position alignment. Filtering can eliminate these potentially confounding
matches (e.g., hits against proline-rich regions or poly-A tails) from the
blast reports, leaving regions whose blast statistics reflect the specificity
of their pairwise alignment.

BLASTN 2.0.11 [Jan-20-2000]
Reference: Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schaffer,
Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997),
"Gapped BLAST and PSI-BLAST: a new generation of protein database search
programs",  Nucleic Acids Res. 25:3389-3402.
Query= RESECO BLAST
UTILITY:\\r5840\pub\MolTox\blast\TRIMMED\MB2D\M2r02_NV.SEQ
         (561 letters)
Database: nt
           607,850 sequences; 1,816,255,750 total letters
---------------------------------------------------------------------------
-
                                                                  Score     E
Sequences producing significant alignments:
gi|3228368|gb|K02061.1|MUSRPL4A  Mus musculus L32-4A pseudog...   565  e-159
gi|6981481|ref|NM_013226.1||  Rattus norvegicus ribosomal pr...   452  e-125

---------------------------------------------------------------------------
gi|3228368|gb|K02061.1|MUSRPL4A Mus musculus L32-4A pseudogene, complete seq
           Length = 1516
Score =  565 bits (285), Expect = e-159
 Identities = 360/384 (93%), Gaps = 5/384 (1%)
 Strand = Plus / Minus
Query: SEQ ID NO: 1
      38    gcaggttttgtgattttatttaaacataaaacatgcacacaagccatctactcattttct 97
            ||||||||||||||||||||||||||||||||||||||||||||||||||| |||||||||
Sbjct: SEQ ID NO: 2
      1094 gcaggttttgtgattttatttaaacataaaacatgcacacaagccatctattcattttct 1035
Query: 98   tcgctgcgtancctggcgttgggattggtgactctgatggccagctgtgctgctctttct 157
            |||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 1034 tcgctgcgtagcctggcgttgggattggtgactctgatggccagctgtgctgctctttct 975
Query: 158  acaatggcttttcagttcttanaggacacattgtgagcaatctcagcacagtaagatttg 217
            ||||||||||||| ||||||| ||||||||||||||||||||||||||||||||||||
Sbjct: 974  acaatggcttttcggttcttagaggacacattgtgagcaatctcagcacagtaagatttg 915
Query: 218  ttgcacatcagcagcacctccagctccttgacattgtggaccannaacttgcggaanccg 277
```

```
                ||||||||||||||||||||||||||||||||||||||||||||||||  ||||||||||| |||
Sbjct: 914  ttgcacatcagcagcacctccagctccttgacattgtggaccaggaacttgcggaagccg 855
Query: 278  ctgggcagcatgtgcttggttttcttgttgctcccacaaccgaagtttnggcatcangat 337
            |||||||||||||||||||||||||||||||||||||||| |||||| | || ||||||| |||
Sbjct: 854  ctgggcagcatgtgcttggttttcttgttgctcccataaccgatg-ttgggcatcaggat 796
Query: 338  ntggcccttgaaccttctcc-ccncctgttgtcnatgcctctgggtttccnc--atttcn 394
             |||||||||||||||||| |  |||||||| ||||||||||||||||| |   ||||
Sbjct: 795  ctggcccttgaaccttctccgcaccctgttgtcaatgcctctgggtttccgccagtttcg 736
Query: 395  cttaa-tttcccatatcggtctga 417
             ||||| |||| ||||||||||||
Sbjct: 735  cttaattttcacatatcggtctga 712
```

gi|6981481|ref|NM_013226.1|| Rattus norvegicus ribsml protein L32(Rpl32), mRNA

```
          Length = 465
Score =  452 bits (228), Expect = e-125
 Identities = 319/350 (91%), Gaps = 2/350 (0%)
 Strand = Plus / Minus
Query: SEQ ID NO: 3
       38  gcaggttttgtgattttatttaaacataaaacatgcacacaagccatctactcatttct 97
           |||| |||||||| |||||||| |||| |||||| |||||||||||||||| ||||| |||
Sbjct: SEQ ID NO: 4
       461 gcagtttttgtggttttatttgaacacaaaacaggcacacaagccatctattcattctct 402
Query: 98  tcgctgcgtancctggcgttgggattggtgactctgatggccagctgtgctgctctttct 157
           |||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 401 tcgctgcgtagcctggcgttgggattggtgactctgatggccagctgtgctgctctttct 342
Query: 158 acaatggcttttcagttcttanaggacacattgtgagcaatctcagcacagtaagatttg 217
           || |||||||||| ||||||| ||||||||||||||||||||||||||||||||||||
Sbjct: 341 acgatggcttttcggttcttagaggacacattgtgagcaatctcagcacagtaagatttg 282
Query: 218 ttgcacatcagcagcacctccagctccttgacattgtggaccannaacttgcggaanccg 277
           |||||||||||||||| ||||||||||||||||||||||  ||||| ||||| |||
Sbjct: 281 ttgcacatcagcagcacttccagctccttgacattgtggaccagaaacttccggaagccg 222
Query: 278 ctgggcagcatgtgcttggttttcttgttgctcccacaaccgaagtttnggcatcangat 337
           || |||||||||||||||||||||||| ||||| |||| ||  || ||||||| |||
Sbjct: 221 ctaggcagcatgtgcttggttttcttgttactcccgtaacc-aatgttgggcatcaggat 163
Query: 338 ntggcccttgaaccttctcc-ccncctgttgtcnatgcctctgggtttcc 386
            |||||||||| ||||||| |  |||||||| ||||||||||||||||
Sbjct: 162 ctggcccttgaatcttctccgcaccctgttgtcgatgcctctgggtttcc 113
```

```
  Database: nt
    Posted date:  Mar 30, 2000 10:02 PM
  Number of letters in database: 1,816,255,750
  Number of sequences in database:  607,850

Lambda     K      H
    1.37    0.711     0.00
Gapped
Lambda     K      H
    1.37    0.711 4.94e-324
Matrix: blastn matrix:1 -3
Gap Penalties: Existence: 5, Extension: 2
Number of Hits to DB: 420761
Number of Sequences: 607850
Number of extensions: 420761
Number of successful extensions: 34073
Number of sequences better than 10.0: 52
```

```
length of query: 561
length of database: 1,816,255,750
effective HSP length: 20
effective length of query: 541
effective length of database: 1,804,098,750
effective search space: 976017423750
effective search space used: 976017423750
T: 0
A: 0
X1: 6 (11.9 bits)
X2: 10 (19.8 bits)
S1: 12 (24.3 bits)
S2: 19 (38.2 bits)
```

The label for Table 3. at page 20, line 8, has been amended as follows:

Table 3. (SEQ ID NO: 5)

The paragraph at page 24, line 7 has been amended as follows:

A vector file must be customized for a particular laboratory and selected prior to the trimming step. The vectors files are formatted using a six line, ASCII text format. Only the first contiguous string of letters on each line is read, so the remainder of each line can be used for annotations. Each line starts with a nucleotide sequence. An example vector file is presented below (SEQ ID NOS 6-11, respectively in order of appearance):

AGCGGCCGCCCGGGCAGGTC // positive insertion orientation 5' adapter sequence

ACCTCGGCCGCGACCACGCT // positive insertion orientation 3' adapter sequence

TTACTAGTGGATCCGAGCTCGGTACCAAGCTTC // forward direction confirm fragment 25 bases after 3' adapter

AGCGTGGTCGCGGCCGAGGT // negative insertion orientation 5' adapter sequence

ACCTGCCCGGGCGGCCGCTC // negative insertion orientation 3' adapter sequence

CACACTGGCGGCCGCTCGAGCATGCATCTAGAG // reverse direction confirm fragment 25 bases after 3' adapter.